Access DB# 83264

11A16

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Lynda Guo Examiner #: 79756 Date: 12/30/02
Art Unit: 1651 Phone Number 30 605-1200 Serial Number: 10/070,018
Mail Box and Bldg/Room Location 11B01-mail 11A16 - office Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Novel target for antiparasitic agents and inhibitors thereof

Inventors (please provide full names): ____________

Earliest Priority Filing Date: ____________

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Point of Contact:
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

STAFF USE ONLY

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher	M. Smith	NA Sequence (#)		STN	
Searcher Phone #		AA Sequence (#)		Dialog	
Searcher Location		Structure (#)		Questel/Orbit	
Date Searcher Picked Up	1/2/03	Bibliographic	X	Dr.Link	
Date Completed	1/17/03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time	60	Fulltext		Sequence Systems	
Clerical Prep Time		Patent Family		WWW/Internet	
Online Time	60	Other		Other (specify)	

PTO-1590 (8-01)

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[illegible] Files
File [illegible]:MEDLINE(R) [illegible] Jan W1
File [illegible]:Biosis Previews(R) [illegible] Jan W1
         (c) [illegible] BIOSIS
File [illegible]:AGRICOLA [illegible] Jan
         (c) format only [illegible] The Dialog Corporation
File [illegible]:SciSearch(R) Cited Ref Sci [illegible] Jan W1
         (c) [illegible] Inst for Sci Info
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         (c) [illegible] ProQuest Info&Learning
File [illegible]:CAB Abstracts [illegible] Dec
         (c) [illegible] CAB International
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         (c) [illegible] Elsevier Science B.V.
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         (c) [illegible] Elsevier Science B.V.
File [illegible]:JICST-EPlus 1985-[illegible] Nov W1
         (c)[illegible] Japan Science and Tech Corp [illegible]
File [illegible]:General Sci Abs Full-Text [illegible] Dec
         (c) [illegible] The HW Wilson Co.
File 144:Pascal 1973-[illegible] Jan W1
         (c) [illegible] INIST [illegible]
File 149:TGG Health&Wellness DB(SM) [illegible] Dec W1
         (c) [illegible] The Gale Group
File [illegible]:ToxFile 1965-[illegible] Nov W3
         (c) format only [illegible] The Dialog Corporation
File 162:CAB Health 1983-2003/Dec
         (c) 2003 CAB International
File 185:Zoological Record Online(R) 1978-[illegible]/Dec
         (c) 2002 BIOSIS
File 340:CLAIMS(R)/US Patent 1950-03/Jan 14
         (c) 2003 IFI/CLAIMS(R)
File 351:Derwent WPI 1963-2002/UD,UM &UP=200303
         (c) 2003 Thomson Derwent
File 357:Derwent Biotech Res. 1982-2003/Jan W1
         (c) [illegible] Thomson Derwent & ISI
File [illegible]:Current BioTech Abs [illegible]-2002/Dec
         (c) 2002 DECHEMA
File 434:SciSearch(R) Cited Ref Sci 1974-[illegible]/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2003/Jan [illegible]
         (c) 2003 Inst for Sci Info
?ds

Set     Items   Description
S1      48955   (PARASIT? OR FUNG? OR BIOCID? OR INSECT? OR BACTER?) AND (-
             SCREEN? OR ASSAY? OR TEST?) AND (PHOSPHATE? OR PHOSPHATASE?
S2     [illegible]   [illegible] AND ENZYME? S, INHIB? OR SUPPRESS?
S3     [illegible]   S1 AND ENZYME?(S(ACTIV? OR INHIB? OR SUPPRESS?)
S4        [illegible]   S3 AND (WORM? OR PROTOZOA? OR NEMATODE? OR MITE?
S5        [illegible]   RD (unique items)
S6         [illegible]   S5 AND (TREHALOSE W,6 [illegible] GLYCEROL [illegible] OR MANNITOL [illegible] [illegible]-
               [illegible]ITOL W,6,W (PHOSPHATE?)
S7         [illegible]   RD (unique items)
[illegible] 1-[illegible]

[illegible] from file: [illegible]
DIALOG(R)File [illegible]:Biosis Previews(R)
[illegible] BIOSIS. All rts. reserv.

[illegible] BIOSIS NO.: [illegible]
[illegible] Trypanosoma [illegible]
```

[illegible]

TITLE: [illegible] of a novel [illegible] 2-amino-N6-substituted [illegible]
AUTHOR: [illegible]; [illegible]; [illegible]; [illegible]
; Van [illegible] Wesley [illegible]; Verlinde Christophe L M J; [illegible]
[illegible]
AUTHOR ADDRESS: [illegible] Department of Chemistry, University of Washington,
Seattle, WA, [illegible]
JOURNAL: Journal of Medicinal Chemistry [illegible] 4[illegible]-4[illegible] November [illegible],
[illegible]
MEDIUM: print
ISSN: [illegible]
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: As part of a project aimed at structure-based design of adenosine analogues as drugs against African trypanosomiasis, N6-, 2-amino-N6-, and N2-substituted adenosine analogues were synthesized and tested to establish structure- activity relationships for inhibiting Trypanosoma brucei glycosomal phosphoglycerate kinase (PGK), glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and glycerol - 3 - phosphate dehydrogenase (GPDH). Evaluation of X-ray structures of parasite PGK, GAPDH, and GPDH complexed with their adenosyl-bearing substrates led us to generate a series of adenosine analogues which would target all three enzymes simultaneously. There was a modest preference by PGK for N6-substituted analogues bearing the 2-amino group. The best compound in this series, 2-amino-N6-[2"-(p-hydroxyphenyl)ethyl]-adenosine (46b), displayed a 23-fold improvement over adenosine with an IC50 of [illegible] muM. 2-[[2"-(p-Hydroxyphenyl)ethyl]amino]adenosine (46c) was a weak inhibitor of T. brucei PGK with an IC50 of 500 muM. To explore the potential of an additive effect that having the N6 and N2 substitutions in one molecule might provide, the best ligands from the two series were incorporated into N6,N2-disubstituted adenosine analogues to yield N6-(2"-phenylethyl)-2-[(2"-phenylethyl)amino]adenosine (69) as a 31 muM inhibitor of T. brucei PGK which is [illegible]-fold more potent than the adenosine template. In contrast, these series gave no compounds that inhibited parasitic GAPDH or GPDH more than 10-20% when tested at 1.0 mM. A 3.0 ANG X-ray structure of a T. brucei PGK/46b complex revealed a binding mode in which the nucleoside analogue was flipped and the ribosyl moiety adopted a syn conformation as compared with the previously determined binding mode of ADP. Molecular docking experiments using QXP and SAS program suites reproduced this "flipped and rotated" binding mode.

2001

AB 2 Item 2 from file: 5
DIALOG(R)File 5:Biosis Previews(R)

[illegible] BIOSIS NO.: [illegible]
AN IMPROVED PURIFICATION OF GLYCOSOMES FROM THE [illegible] TRYPOMASTIGOTES OF TRYPANOSOMA-BRUCEI
AUTHOR: AMAN R A; WANG C C
AUTHOR ADDRESS: DEP. MED. MICROBIOL., STANFORD UNIV. SCH. MED., STANFORD, CA.
JOURNAL: MOL BIOCHEM PARASITOL 21 [illegible]. 1986. [illegible]
FULL JOURNAL NAME: Molecular and Biochemical Parasitology
CODEN: MBIPD
RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The glycosomes of in vitro grown procyclic trypomastigote forms of Trypanosoma brucei were purified by three different procedures and the results compared by electron microscopy, enzyme assays and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Centrifugation on a [illegible] Percoll gradient followed by a sucrose gradient centrifugation resulted in the least enriched glycosomal preparation. Centrifugation on a pre-formed Nycodenz gradient gave an improved preparation but the most homogeneous preparation of intact glycosomes was obtained after centrifugation on two successive sucrose gradients. Glycosomes purified by both the Nycodenz and double sucrose gradient procedures appeared larger than in situ glycosomes presumably due to an osmotic effect resulting from disruption of the granular matrix of the organelles. Nevertheless, there appears to be no loss of internal contents due to the swelling of the organelles. The glycosomes of the blood stream form trypomastigotes purified by the same procedure show, however, no sign of swelling. A comparison of glycosomes purified from procyclic trypomastigotes and bloodstream form trypomastigotes prepared by the same double sucrose procedure demonstrated that in the glycosomes of procyclic trypomastigotes: (1) activities of hexokinase, phosphoglucose isomerase, phosphofructokinase, aldolase and phosphoglycerate kinase are diminished by [illegible]; (2) activities of glyceraldehyde-3-phosphate dehydrogenase, triose phosphate isomerase and glycerol-3-phosphate dehydrogenase remain unchanged or are only slightly reduced; (3) there is an appearance of four major new proteins, among which could be phosphoenol pyruvate carboxykinase and malate dehydrogenase. These observations are in basic agreement with those by Hart et al. (Mol. Biochem. Parasitol. 12, 25-35, 1984).

1986

7/AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

[illegible] BIOSIS NO.: 0000740194[illegible]
LOCALIZATION OF MALATE DEHYDROGENASE EC-1.1.1.37 ADENYLATE KINASE EC-2.7.4.3 AND GLYCOLYTIC ENZYMES IN GLYCOSOMES AND THE THREONINE PATHWAY IN THE MITOCHONDRION OF CULTURED PROCYCLIC TRYPOMASTIGOTES OF TRYPANOSOMA-BRUCEI
AUTHOR: OPPERDOES F R; MARKOS A; STEIGER R F
AUTHOR ADDRESS: RESEARCH UNIT FOR TROPICAL DISEASES, INTERNATIONAL INST. OF CELLULAR AND MOLECULAR PATHOLOGY, ICP, AVENUE HIPPOCRATE 74, B-1200 BRUSSELS, BELGIUM.
JOURNAL: MOL BIOCHEM PARASITOL 4 (5-6). 1981 (RECD. 198[illegible]). 291-31[illegible]. 1981
FULL JOURNAL NAME: Molecular and Biochemical Parasitology
CODEN: MBIPD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Procyclic culture forms of the human and cattle parasite T. brucei stock 427 were screened for the presence of enzymes involved in glycolysis, mitochondrial energy metabolism and threonine degradation. The enzyme activities in the procyclics were compared with those of the bloodstream forms. The specific activities of glycolytic enzymes represented [illegible] of the respective levels in the bloodstream form, except for hexokinase (EC 2.7.1.1) which was [illegible]-fold reduced. [illegible] was that the enzymes involved in the early [illegible] of the glycolytic pathway, i.e., from hexokinase to phosphoglycerate kinase (EC 2.7.2.3) and the enzymes NAD-linked glycerol-3-phosphate [illegible]

[illegible]kinase (EC 1.1.1.[illegible]) and glycerol kinase were all present in glycosomes equilibrating at a density of 1.[illegible] g/ml in sucrose gradients. Malate dehydrogenase was [illegible]-fold more active in procyclics than in bloodstream forms. This increase in activity was the result of the appearance of malate dehydrogenase in the glycosomes of the procyclics, in addition to mitochondrial and cell-sap activities which were present in both stages of the life cycle. Glycosomes contained part of the adenylate kinase activity, which was also associated with the mitochondrion. Succinate dehydrogenase (EC 1.3.99.1) and sn- glycerol - 3 - phosphate dehydrogenase (EC 1.1.99.5), together with oligomycin-sensitive ATPase (EC 3.6.1.3), were located in the mitochondrion which had a density in sucrose ranging from 1.1[illegible]-1.1[illegible] g/ml. This organelle also contained L-threonine 3-dehydrogenase (EC 1.1.1.103) and carnitine acetyltransferase (EC 2.3.1.7), 2 enzymes involved in threonine catabolism. The latter 2 enzymes had activities which were, respectively, 15- and 13-fold higher in the procyclics than in the bloodstream form. Mitochondrial sn- glycerol - 3 - phosphate dehydrogenase was decreased 4-fold.

1981

7/AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02817866 BIOSIS NO.: 000069026084
TREHALOSE 6 PHOSPHATE SYNTHASE EC-2.4.1.15 FROM DICTYOSTELIUM-DISCOIDEUM PARTIAL PURIFICATION AND CHARACTERIZATION OF THE ENZYME FROM YOUNG SOROCARPS
AUTHOR: KILLICK K A
AUTHOR ADDRESS: DEP. DEV. BIOL., BOSTON BIOMED. RES. INST., BOSTON, MASS. 02114, USA.
JOURNAL: ARCH BIOCHEM BIOPHYS 196 (1). 1979. 121-133. 1979
FULL JOURNAL NAME: Archives of Biochemistry and Biophysics
CODEN: ABBIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Trehalose 6 - phosphate synthase was solubilized from young sorocarps of the cellular slime mold, D. discoideum, by a freeze-thaw cycle and was subsequently purified about 160-fold using streptomycin sulfate precipitation, $(NH_4)_2SO_4$ fractionation, DEAE-cellulose chromatography, heat treatment in the presence of heparin and molecular sieve chromatography on columns of Bio-Gel A-1.5 m. The purified enzyme was maximally active at pH 6.5, showed an absolute specificity for G-6-P as glucosyl acceptor and a relative specificity for the glucosyl donor in the order: UDP-glucose, GDP-glucose and ADP-glucose. Although heparin and chondroitin sulfate activated the synthase, the order of glucosyl donor specificity was not affected. Other activators of trehalose 6 - phosphate synthase were KCl, Mg^{2+} and EDTA, while detergents had little effect. Although synthase activity was reduced [illegible] to [illegible] upon the omission of Mg^{2+} from the assay mixture, an absolute dependency for Mg^{2+} could not be demonstrated. Evaluation of the apparent Km values for partially purified synthase preparations demonstrated that for each of the synthase substrates, the Lineweaver-Burk plots displayed complex bimodal kinetics. Estimation of the Km after extrapolation of the straight line portions of these plots yielded values of [illegible] and [illegible] mM G-6-P and [illegible] and [illegible] mM UDP-glucose. Comparison of the latter parameters with the cellular levels of UDP-glucose and G-6-P in Dictyostelium suggests that if the observed bimodal kinetics are the consequence of multiple kinetically distinct forms of the synthase, the activation [illegible]

[illegible]

[illegible]

AUTHOR: FAIRLAMB A H; BOWMAN I B R
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. EDINB. MED. SCH., TEVIOT PL., EDINBURGH EH8 9AG, SCOTL., UK.
JOURNAL: EXP PARASITOL 43 (1). 1977. RECD 1977. 88-93. 1977
FULL JOURNAL NAME: Experimental Parasitology
CODEN: EXPAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A number of chemotherapeutic compounds effective against T. brucei were tested as inhibitors of the purified glycerophosphate oxidase (sn- glycerol - 3 - phosphate : oxygen oxidoreductase). Melarsen oxide and suramin were potent inhibitors of the dehydrogenase component of this multienzyme complex. Suramin is a potent competitive inhibitor of the oxidase with a Ki of 4.1 .mu.M with respect to glycerophosphate. The Km for glycerophosphate for the enzyme decreased from 6.8 to 1.7 mM in the presence of bovine serum albumin while the Vmax was increased 2- to 3-fold. Human and bovine serum albumin can protect the oxidase from inhibition by suramin, by preferential binding of the drug. Analogs of suramin with little or no chemotherapeutic value are less effective inhibitors of the oxidase, and the correlation between therapeutic action and potency as inhibitors suggests that this enzyme is 1 of the principal sites of action of suramin in vivo.

19 [illegible]

[illegible] Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

[illegible] BIOSIS NO.: 000064041079
A RADIOMETRIC ASSAY FOR TREHALOSE 6 PHOSPHATE SYNTHETASE EC-2.4.1.15
AUTHOR: KILLICK K A
JOURNAL: ANAL BIOCHEM 79 (1-2). 1977 310-314. 1977
FULL JOURNAL NAME: Analytical Biochemistry
CODEN: ANBCA
RECORD TYPE: Abstract

ABSTRACT: A specific and sensitive radiometric assay was developed for the measurement of trehalose - 6 - phosphate (trehalose-6-P synthetase (EC 2.4.1.15, Dictyostelium discoideum) activity. With either [illegible] or UDP-[14C]glucose as substrate, products unique to the synthetase reaction, i.e., trehalose-6-P and trehalose, may be quantitated after charcoal column chromatography by either paper [illegible] electrophoresis or TLC. [illegible] of this assay [illegible] synthetase activity [illegible] based on nucleoside diphosphate [illegible]

[illegible]

[illegible] specificity; no other enzyme besides the synthetase catalyzes the synthesis of [illegible]; greater sensitivity at low levels of [illegible]; and insensitivity to competing side reactions known to interfere with the [illegible] assay (e.g., [illegible] phosphorylase-catalyzed synthesis of polymerization of [illegible]).

[illegible] (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

[illegible] H.W. WILSON RECORD NUMBER: BGSA[illegible]
Channeling of substrates and intermediates in enzyme-catalyzed reactions.
Huang, Xinyi
Holden, Hazel M; Raushel, Frank M
Annual Review of Biochemistry v. [illegible] p. [illegible]
SPECIAL FEATURES: bibl il ISSN: [illegible]-4154
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: [illegible]

ABSTRACT: The three-dimensional structures of tryptophan synthase, carbamoyl phosphate synthetase, glutamine phosphoribosylpyrophosphate amidotransferase, and asparagine synthetase have revealed the relative locations of multiple active sites within these proteins. In all of these polyfunctional enzymes , a product formed from the catalytic reaction at one active site is a substrate for an enzymatic reaction at a distal active site. Reaction intermediates are translocated from one active site to the next through the participation of an intermolecular tunnel. The tunnel in tryptophan synthase is {similar}25 A in length, whereas the tunnel in carbamoyl phosphate synthetase is nearly 100 A long. Kinetic studies have demonstrated that the individual reactions are coordinated through allosteric coupling of one active site with another. The participation of these molecular tunnels is thought to protect reaction intermediates from coming in contact with the external medium. Reprinted by permission of the publisher.

7/AB/2 (Item 2 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

04108242 H.W. WILSON RECORD NUMBER: BGSI99108242
Experimental evolution and its role in evolutionary physiology.
Bennett, Albert F
Lenski, Richard E
American Zoologist (Am Zool) v. 39 no2 (Apr. 1999) p. 346-62
SPECIAL FEATURES: bibl il ISSN: 0003-1569
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: [illegible]

ABSTRACT: Four general approaches to the study of evolutionary physiology--phylogenetically-based comparisons, genetic analyses and manipulation, phenotypic plasticity and manipulation, and selection studies--are outlined and discussed. We provide an example of the latter, the application of laboratory selection experiments to the study of a problem area in environmental adaptation, differences in adaptive patterns of generalists and specialists. A line of the bacterium [illegible] that had evolved in a constant environment of [illegible] was replicated

[illegible] and allowed to [illegible] fluctuations in a [illegible] thermal environment alternating between [illegible]. As predicted by theory, fitness and efficiency [illegible] this new environment, as did stress resistance. Contrary to predictions, however, fitness and efficiency in the [illegible] thermal environment [illegible] increase, but did thermal [illegible] [illegible] experiment [illegible] hypotheses and assumptions [illegible]. Reprinted by permission of the publisher.

[illegible] Item [illegible] from file: 149
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

[illegible] SUPPLIER NUMBER: [illegible] (USE FORMAT 7 OR 9 FOR FULL TEXT)
Changes in membrane polar lipid fatty acids of seashore paspalum in response to low temperature exposure. (Turfgrass Science).
[illegible], [illegible]; [illegible], [illegible]; Duncan, R.R.; Baird, W.V.
Crop Science, 4[illegible], [illegible], [illegible]
[illegible],

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: [illegible]
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic; Trade
WORD COUNT: [illegible] LINE COUNT: [illegible]

AUTHOR ABSTRACT: Seashore paspalum (Paspalum vaginatum Sw.) is a warm-season turfgrass, best known for its superior salt tolerance. Plants are subject to injury during winter conditions along the northern boundary of their zone of adaptation. New cultivars that are more tolerant to low temperatures are needed for use in the transition zone. Cold tolerance has been correlated with the degree of unsaturation in membrane lipid fatty acids. Unsaturated fatty acids are thought to aid in maintaining membranes in a fluid state necessary for biological functioning (homeophasic adaptation). The primary objective was to characterize fatty acid composition of membrane lipids in three genotypes differing in cold tolerance. A second objective was to investigate changes in fatty acid content in these genotypes during exposure to low temperatures. Cold-treated plants were exposed to a 1[illegible]-h photoperiod at [illegible](degrees)/14(degrees)C day/night temperatures and light intensity of [illegible] (micro mol m.sup.-2 s.sup.-1) photosynthetic photon flux density for [illegible] wk. Rhizomes and crowns were harvested at [illegible]-d intervals. Total lipids were extracted and the polar lipids separated by thin-layer chromatography. Fatty acids were identified by gas chromatography (GC) and mass spectroscopy. In all three genotypes, the two saturated fatty acids, palmitic acid and stearic acid, did not change during cold treatment. The triunsaturated linolenic acid increased significantly during low temperature exposure. The magnitude of change was greater in the finer-textured and more cold-tolerant PI [illegible] ('Sealsle[illegible]'), than in the intermediately cold-tolerant 'Adalayd' or in the cold-susceptible, coarse-textured PI [illegible]. These findings suggest that accumulation of linolenic acid partly explains the differential response in their cold tolerance.

[illegible] Item [illegible] from file: 351
DIALOG(R)File 351:Derwent WPI

[illegible]
WPI [illegible]: [illegible]

[illegible]

Related WPI Acc No: [illegible]
XRAM Acc No: [illegible]
Assessing candidate inhibitors of sugar/sugar alcohol phosphatases [illegible] and antifungals [illegible] comprises measuring the enzyme activity in the presence of the candidate inhibitor
Patent Assignee: LEUVEN RES & DEV (LEUV-N)
Inventor: THEVELEIN J; VAN DIJCK P
Number of Countries: [illegible] Number of Patents: [illegible]
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
[illegible]	A1	[illegible]	EP [illegible]	A	[illegible]	[illegible] B

Priority Applications (No Type Date): EP [illegible] A [illegible]
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP [illegible]	A1	E	[illegible]	[illegible]	

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
Abstract (Basic): EP [illegible] A1
Abstract (Basic):

NOVELTY - Assessing substances as direct/indirect inhibitors of sugar/sugar alcohol phosphatases in cells where the sugar/sugar alcohols accumulate e.g. stress or abnormal conditions, comprises:

(a) Measuring the enzyme activity in the presence of the inhibitor and sugar/sugar alcohol phosphate in a biological medium; and

(b) Determining that the substance is an inhibitor if the enzyme activity is reduced.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an inhibitor obtained by the method of the invention.

USE - The method is used to isolate inhibitors of sugar/sugar alcohol phosphatases and lead to a cytotoxic build up of an intermediate normally produced under conditions of stress (claimed). The inhibitor can be used as a biocide along with an antifungal agent e.g. an azole (claimed).

ADVANTAGE - The inhibitors have a novel mechanism of action compared to known anti-fungals and would therefore be less likely to encounter resistance among pathogenic fungi. Known antifungals often have undesirable side-effects e.g. toxicity to mammalian cells which would not be encountered with the new inhibitors.

pp; 28 DwgNo 0/9

[illegible]AB 11 Item 2 from file: 351
DIALOG(R)File 351:Derwent WPI

[illegible]
WPI Acc No: [illegible]/200124
Related WPI Acc No: 2001-246803
XRAM Acc No: [illegible]481
New inhibitors and screening assay for inhibitors or suppressors of sugar alcohol phosphatases or sugar phosphatases
Patent Assignee: LEUVEN RES & DEV (LEUV-N)
Inventor: THEVELEIN J; VAN DIJCK P
Number of Countries: [illegible] Number of Patents: [illegible]
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO [illegible]	A[illegible]	[illegible]	WO [illegible]	A	[illegible]	[illegible] B
AU [illegible]	A	[illegible]	AU [illegible]	A	[illegible]	[illegible]
[illegible]	A[illegible]	[illegible]	EP [illegible]	A	[illegible]	[illegible]
			WO [illegible]	A	[illegible]	

Priority Applications (No Type Date): EP [illegible] A [illegible]; EP [illegible] A [illegible]

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

[illegible]

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY [illegible]

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT [illegible]

[illegible] Based on patent WO [illegible]

[illegible] Based on patent WO [illegible]

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

Abstract (Basic): WO [illegible] A1

Abstract (Basic):

NOVELTY - A screening assay for inhibitors or suppressors of sugar alcohol phosphatases or sugar phosphatases using enzymes from e.g. fungi, bacteria, insects, nematodes, mites or protozoa, is new.

DETAILED DESCRIPTION - A method for assessing the activity of test substances as inhibitors of a first cell enzyme converting a sugar phosphate into a sugar, or a sugar alcohol phosphate into a sugar alcohol in cells. The sugar or sugar alcohol is accumulated in large quantities by the cells, e.g. under conditions deviating from the optimal growth condition of the target cells or as a reaction to stress conditions, the inhibition being directly of the first enzyme or indirectly. The method comprises:

(a) contacting a test compound with a biological medium comprising the sugar phosphate or sugar alcohol phosphate and the first enzyme;

(b) measuring the activity in the medium which depends on the activity of the first enzyme;

(c) repeating steps (1) and (2) with further test compounds; and

(d) selecting at least 1 compound which reduces activity of the enzyme compared with the same medium without the inhibitor; and

(e) (optionally) assessing the activity of a second cell enzyme which is involved in the synthesis of the corresponding sugar phosphate or sugar alcohol phosphate.

The selecting step includes selection of inhibitors which reduce the activity of the first enzyme while maintaining a viable activity of the second enzyme.

INDEPENDENT CLAIMS are included for the following:

(1) inhibitors identified by the above method;

(2) preparations comprising 1 or more of the inhibitors;

(3) a biocide acting on fungi, insects, nematodes, bacteria or other organisms accumulating large quantities of sugar alcohol or a sugar in response to stress, comprising the inhibitors;

(4) a method of increasing the sugar phosphate or sugar alcohol phosphate content in a target cell, particularly a mammalian parasite, comprising using an inhibitor to reduce the activity of a first cell enzyme converting a sugar phosphate into a sugar or sugar alcohol phosphate into a sugar alcohol; and

(5) a method of reducing or impairing the pathogenicity of a mammalian parasite by promoting hyper-accumulation of a sugar phosphate or a sugar alcohol phosphate.

ACTIVITY - Antiparasitic; [illegible]; [illegible]; [illegible]; [illegible].

MECHANISM OF ACTION - Trehalose - 6 - phosphate phosphatase [illegible]

[illegible]

[illegible]

[illegible]

Various concentrations of test compounds were applied to [illegible] hyphae [illegible], and [illegible] inhibitory activity [illegible] was calculated. Test compound II had an [illegible] [illegible].

[illegible] compounds [illegible] are useful [illegible] parasitic [illegible], particularly fungal, [illegible] in a human, animal or plant.

[illegible]

Scanned by [illegible]

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=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 10:40:17 ON ... 03
USE IS SUBJECT TO THE TERMS OF YOUR STN ... AGREEMENT.
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COPYRIGHT (C) 200. AMERICAN CHEMICAL ... CS
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FILE COVERS 1907 - 17 Jan 2003 VOL 13. ... 4
FILE LAST UPDATED: 16 Jan 2003 (20030...)
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This file contains CAS Registry Numbe... easy and accurate substance identification.

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=> d stat que
L1          39 SEA FILE=REGISTRY TREHA...-PHOSPHATE?/CN
L2         195 SEA FILE=REGISTRY GLYC...-PHOSPHATE?/CN
L3          23 SEA FILE=REGISTRY MANN...-PHOSPHATE?/CN
L4           5 SEA FILE=REGISTRY SORB...-PHOSPHATE?/CN
L6           1 SEA FILE=REGISTRY ERYTH... -4-PHOSPHATE?/CN
L7          1. SEA FILE=REGISTRY SUGA...PHATE?/CN
L8         32. SEA FILE=HCAPLUS L1 OR ...E(W)6(W)PHOSPHATE?
L9        5865 SEA FILE=HCAPLUS L2 OR ...(W)3(W)PHOSPHATE?
L10        231 SEA FILE=HCAPLUS L3 OR ...(W)1(W)PHOSPHATE?
L11        11. SEA FILE=HCAPLUS L4 OR ...(W)6(W)PHOSPHATE?
L12          . SEA FILE=HCAPLUS ARABI... (W)PHOSPHATE?
L13         98 SEA FILE=HCAPLUS ERYTHR... (W)4(W)PHOSPHATE? OR L6
L14       3083 SEA FILE=HCAPLUS L7 OR ... (W)PHOSPHATE?
L15      69967 SEA FILE=HCAPLUS (?PARA... F FUNG? OR BIOCID? OR ?INSECT?)
                AND (SCREEN? OR ASSAY? ...)
L16      10036 SEA FILE=HCAPLUS PHOSPHAT... PHOSPHATASE? OR SUGAR(W)PHOSPHATAS
                E? OR L8 OR L9 OR L10 ... L12 OR L13 OR L14
L17         71 SEA FILE=HCAPLUS L15 AN...
L18         52 SEA FILE=HCAPLUS L17 AN... ENZYME?
L19         15 SEA FILE=HCAPLUS L18 AN... OR BACTER? OR PROTOZOA? OR
                NEMATODE? OR MITE?)
```

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=> d ibib abs hitrn l19 1-15

L19 ANSWER 1 OF 15 HCAPLUS COPYRIGH... ACS
ACCESSION NUMBER:        2002:695799 ...
DOCUMENT NUMBER:         137:226941
TITLE:                   Use of certai... for treatment of a number of
                         conditions in ... blood cell deficiencies
INVENTOR(S):             Ahlem, Claren...; Reading, Christopher; Frincke,
                         James; St...; Lardy, Henry; Marwah, Padma;
                         Marwah, Ashok; ...gast, Patrick T.
PATENT ASSIGNEE(S):      Hollis-Eden Ph...icals, Inc., USA
```

SOURCE: PCT Int. Appl., [illegible]
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069977	A1	20020912	[illegible]-US6716	[illegible]

W: AE, AG, AL, AM, AT, AU, [illegible], BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, [illegible], EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, [illegible], KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, [illegible], MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, [illegible], SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, [illegible], AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, [illegible], TR, [illegible], LU, AT, BE, CH, CY, DE, DK, ES, FI, FR, [illegible], IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, [illegible], GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
[illegible]1-272624P P 20010301
[illegible]1-820483 A 20010329
[illegible]1-323016P P 20010919
[illegible]1-328738P P 20011011
[illegible]1-340354P P 20011101
[illegible]1-338015P P 20011108
[illegible]1-343523P P 20011220

OTHER SOURCE(S): MARPAT 137:[illegible]

AB The invention relates to the use [illegible] to treat a no. of conditions, such as thrombocytopenia, neutrop[illegible] the delayed effects of radiation therapy. Compds. that can be used [illegible] invention include methyl-2,3,4-trihydroxy-1-O-(7,17-[illegible]androst-5-ene-3.beta.-yl)-.beta.-D-glucopyranosid ronate. Formulati[illegible] the steroids are also exemplified.

IT **9075-65-4**, Glycerophosphate dehyd[illegible]
RL: BSU (Biological study, unclas[illegible]; BIOL (Biological study)
(steroid hormone induction [illegible] of mitochondrial GDPH and cytosolic malic **enzyme** in rat [illegible] synthetic prepn. and use of certain steroids for tr[illegible] of a no. of conditions including blood cell deficiencies)

REFERENCE COUNT: 13 THERE AR[illegible]TED REFERENCES AVAILABLE FOR THIS RECORD. [illegible]ATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 15 HCAPLUS COPYRIGH[illegible]CS
ACCESSION NUMBER: 2002:59878 H[illegible]
DOCUMENT NUMBER: 136:156403
TITLE: Methods for i[illegible]ing therapeutic targets for treating infe[illegible]isease
INVENTOR(S): Shepard, Mich[illegible]; Lackey, David B.; Cathers, Brian E.; Sergeeva, [illegible]
PATENT ASSIGNEE(S): Newbiotics, I[illegible]
SOURCE: PCT Int. Appl., [illegible]
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002... A2 20020131 ... 01-US23198 ...
W: AE, AG, AL, AM, AT, AU, A..., BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, ..., ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, ..., KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, M..., MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, S..., TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, B..., MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, ..., TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, ..., LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, ..., ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: ...

AB This invention provides methods and ... to identify **enzymes** that act as **enzyme**-catalyzed ... activators and the **enzymes** identified by these meth... provided by this invention are compds. activated by ... **enzymes** as well as compns. contg. these compds.

IT **37250-69-4**
RL: BSU (Biological study, unclas...); CAT (Catalyst use); THU (Therapeutic use); BIOL (Biologic...); USES (Uses)
(identifying intrinsic **enzyme**-... therapeutic activators as targets for trea... infectious disease)

IT **9025-72-3**, E.C. 3.1.3.12
RL: CAT (Catalyst use); PRP (Prop...); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identifying intrinsic **enzyme**-... therapeutic activators as targets for trea... infectious disease)

L19 ANSWER 3 OF 15 HCAPLUS COPYRIGHT ... ACS

ACCESSION NUMBER: 2001:865255 ...
DOCUMENT NUMBER: 136:34648
TITLE: Genes, **enzymes**, ...ed intermediates, and methods for an... mevalonate-independent isoprenoid bi... pathway
INVENTOR(S): Adam, Petra; ..., Adelbert; Eisenreich, Wolfgang; Fellermeier, M...; Hecht, Stefan; Rohdich, Felix; Schuhr, Chris...; Wungsintaweekul, Juraithip; Zenk, Meinhart H.
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., ... pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10027821	A1	20011206	...2000-10027821	20000605
WO 2001094561	A2	20011213	...01-EP6255	20010601
WO 2001094561	A3	20020530		

W: AE, AL, AM, AT, AU, AZ, B..., BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ..., GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, K..., LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, ..., PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, ..., UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, ..., TM
RW: GH, GM, KE, LS, MW, MZ, ..., TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, [illegible], LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, [illegible], MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: [illegible]

AB The present invention concerns **enzymes** [illegible] intermediates of the mevalonate-independent isopren[illegible] [illegible] pathway downstream from 2C-methyl-D-erythritol-2,4-cyclo[illegible] [illegible] phate and upstream from isopentenylpyrophosphate or dime[illegible] [illegible] pyrophosphate. These are used for **screening** for inhibitors of th[illegible] **enzymes** and for identification of inhibitor-resist[illegible] [illegible] ants. Further disclosures concern genes coding for the **enzymes** [illegible] inhibitor-resistant variants of the **enzymes**, vectors [illegible] contain the genes, cells which contain the vectors, and pla[illegible] [illegible] contg. such vectors. Thus, the Bacillus subtilis and Escherichi[illegible] [illegible] for the mevalonate-independent isoprenoid biosynthes[illegible] [illegible] were cloned and expressed. The DXP synthase and DXP reducto[illegible] **enzymes** were used to prep. [U-13C5]-2C-methyl-D-**erythritol**-4-**phosphate**. The gene ygiE 1-deoxy-[illegible] -5-phosphate synthase, gene yaeM 1-deoxy-D-xylulose-5-ph[illegible] reductoisomerase, and gene ygbP 4-diphosphocytidyl-2C-methyl-D-er[illegible] synthase were used in prepn. of [2,2-13C2]-4-diphosphocytidyl-2C-[illegible] -erythritol. Genes downstream of ygbP, i.e., gcpE, lytB, yjeE, and [illegible] cloned for use in **screening** for inhibitors of isopr[illegible] synthesis or for prepg. intermediates in the pathway.

L19 ANSWER 4 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER:	2001:816926 [illegible]
DOCUMENT NUMBER:	135:354706
TITLE:	Structure of [illegible] cytidyl methylerythritol synthetase in[illegible] mevalonate-independent isoprenoid bi[illegible] s and the rational design of effectors
INVENTOR(S):	Noel, Joseph [illegible]; [illegible]man, Marianne E.; Richard, Stephane
PATENT ASSIGNEE(S):	The Salk Insti[illegible] r Biological Studies, USA
SOURCE:	PCT Int. Appl., [illegible] pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083769	A2	20011108	[illegible] 2001-US14371	20010503
WO 2001083769	A3	20020829		

W: AE, AG, AL, AM, AT, AU, A[illegible], BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, D[illegible], ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, [illegible], KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, M[illegible], MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, S[illegible], TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, [illegible], MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, S[illegible], TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, G[illegible], LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, G[illegible], MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: [illegible] P 20000503
[illegible] P 2000121[illegible]

AB The present invention provides th[illegible] of the **enzyme** 4-diphosphocytidyl-2-C-methylery[illegible] (CDP-ME) synthase, a member of the cytidyltransferase family of **enzymes**. [illegible]-ME is a crit.

intermediate in the mevalonate-in pathway for isoprenoid biosynthesis in a no. of prokaryo isms, in algae, in the plastids of plants, and in the malaria **parasite**. Since vertebrates synthesize isoprenoid precursors mevalonate pathway, CDP-ME synthase and other **enzymes** of the -independent pathway for isoprenoid prodn. represent targets for the structure-based design of selective antibacteria al, and antimalarial drugs. Accordingly, the present inventi methods for **screening** for compds. that inhibit **enzymes** valonate-independent pathway and pharmaceutical compns. bacterial formulations thereof. Further provided are methods of the **enzymes** of the pathway and **bacterial** terpenoid s and methods for treating a subject suffering from **bacterial** infection.

L19 ANSWER 5 OF 15 HCAPLUS COPYRIGH

ACCESSION NUMBER: 2001:16817

DOCUMENT NUMBER: 134:217175

TITLE: Sugar alcoh ases or **sugar phosphatases** targets for **antiparasitic** and use of the inhibitors in **biocides** an aceuticals

INVENTOR(S): Thevelein, J Dijck, Patrick

PATENT ASSIGNEE(S): K.U. Leuven R Development, Belg.

SOURCE: PCT Int. Appl., p.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.       KIND  DATE          ICATION NO.     DATE
---------------  ----  --------    ---------------  --------
WO 2001016357     A2   20010308     000-EP8410      20000829
WO 2001016357     A3   20011129
    W:  AE, AG, AL, AM, AT, AU, A ,  , E, BG, BR, BY, BZ, CA, CH, CN,
        CR, CU, CZ, DE, DK, DM, L ,  , S, FI, GB, GD, GE, GH, GM, HR,
        HU, ID, IL, IN, IS, JP, KE,  , P, KR, KZ, LC, LK, LR, LS, LT,
        LU, LV, MA, MD, MG, MK, MN,  , X, MZ, NO, NZ, PL, PT, RO, RU,
        SD, SE, SG, SI, SK, SL, TJ,  , R, TT, TZ, UA, UG, US, UZ, VN,
        YU, ZA, AM, AZ, BY, KG, K ,  ,  , TJ, TM
    RW: GH, GM, KE, LS, MW, MZ, S ,  , Z, TZ, UG, ZW, AT, BE, CH, CY,
        DE, DK, ES, FI, FR, GB, GR,  , T, LU, MC, NL, PT, SE, BF, BJ,
        CF, CG, CI, CM, GA, GN, GW,  , R, NE, SN, TD, TG
EP 1081232        A1   20010307       1999-202805   19990830
    R:  AT, BE, CH, DE, DK, ES, FR,  , R, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO
EP 1206568        A2   20020522       000-964054    20000829
    R:  AT, BE, CH, DE, DK, ES, FR,  , R, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK
PRIORITY APPLN. INFO.:                -202805     A   19990830
                                      -70145      A   20000627
                                      -EP841      W   20000829
```

AB The use of an **enzyme** found in **fungi**, **bacteria**, **insects**, **nematodes**, **worms**, **mites**, **protozoa** etc. as a target in a **screening assay** is described by means of wh capable of inhibiting the function of that **enzyme** may b ied. The **screening assay** may include compl or purified-**enzyme assays**. In particular, th invention

relates [illegible] a **screening assay** [illegible] suppressors [illegible] sugar alc. phosph[illegible] **sugar phosphatases**, and more in partic[illegible] [illegible] suppressors [illegible] **trehalose-6-phosphate phosphatase**, as well as prepns., in particular, [illegible] [illegible] prepns., which include inhibitors or suppressors obtain[illegible] [illegible] **screening assay**. Inhibitors are described [illegible] [illegible] applications in **biocides** and antifungal pharma[illegible]

IT **9023-07-8, Sugar phosphatase 9025-72-3, Trehalose-6-phosphate phosphatase 9055-29-2**, Mannitol-1-phosphatase **37228-75-4**, Glycerol-3-phosphatase
RL: BAC (Biological activity or [illegible], except adverse); BPR (Biological process); BSU (Biological study, [illegible] [illegible]ted); BIOL (Biological study); PROC (Process)
(inhibitors; sugar alc. phosph[illegible] **sugar phosphatases** as novel targets [illegible] **antiparasitic** agents and use of inhibitors [illegible] **biocides** and pharmaceuticals)

L19 ANSWER 6 OF 15 HCAPLUS COPYRIGH[illegible]
ACCESSION NUMBER: 2000:742235 [illegible]
DOCUMENT NUMBER: 133:291952
TITLE: Modification [illegible] biosynthesis by DNA shuffling
INVENTOR(S): Yuan, Ling; [illegible], Sun Ai; Lassner, Michael
PATENT ASSIGNEE(S): Maxygen, Inc., [illegible]
SOURCE: PCT Int. Appl., [illegible]
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061740	A1	20001019	[illegible]-US9285	20000406

W: AE, AL, AM, AT, AU, AZ, [illegible], BB, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, [illegible], GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, [illegible], LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, [illegible], PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, [illegible], US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, T[illegible]
RW: GH, GM, KE, LS, MW, SD, S[illegible], UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, [illegible], MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, M[illegible], SN, TD, TG
PRIORITY APPLN. INFO.: [illegible]-128707P P 19990410

AB Methods of modulating lipid prodn. [illegible] and whole organisms by DNA shuffling are provided. Single gen[illegible], operons, lipid biosynthetic cycles and whole genomes can be recombin[illegible] [illegible]duce cells and organisms with desirable lipid synthetic or metab[illegible] [illegible]ivity. Libraries of recombined lipid synthetic nucleic acids and [illegible] are also provided. Modification of lipid satn., fatt[illegible] [illegible]mpn., fatty alc. compn., wax compn., acyl chain length, locat[illegible] [illegible] acid accumulation, triglyceride yield, substrate sp[illegible], expression level, are described. A decrease in suscep[illegible] [illegible] protease cleavage, high or low pH levels, extreme temps., are a[illegible]. A decrease in toxicity, and modification of methyltransferase [illegible] resulting in formation of branched chain, cyclopropyl, meth[illegible] [illegible] fatty acids, are also described. Use of two-hybrid sys[illegible] [illegible]ting the changes in lipid biosynthetic activity is als[illegible] **Screening** [illegible] libraries,

such as phage display library is [illegible]. Crop plants such as corn, peanut, barley, millet, rice, [illegible], wheat, oats, sunflower, [illegible] nut whose lipid biosynthetic [illegible], are claimed. DNA shuffling is a powerful process [illegible] evolution, which generates diversity by recombination, [illegible] mutations in individual genes.

REFERENCE COUNT: 11 THERE [illegible] REFERENCES AVAILABLE FOR THIS RECORD. [illegible] AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER: 2000:[illegible]

DOCUMENT NUMBER: 133:[illegible]

TITLE: The non-meval[illegible] [illegible]prenoid biosynthesis of plants as a **test** sys[illegible] new herbicides and drugs against [illegible] **bacteria** and the malaria **parasite**

AUTHOR S : Lichtenthaler, [illegible] K.; Zeidler, Johannes; Schwender, J[illegible]; [illegible], Christian

CORPORATE SOURCE: Botanisches In[illegible] II, Universitat Karlsruhe, Karlsruhe, D-[illegible], [illegible]many

SOURCE: Zeitschrift [illegible] [illegible]rschung, C: Journal of Biosciences [illegible], [illegible]6), 305-313
CODEN: ZNCBDA; [illegible]: [illegible]-5075

PUBLISHER: Verlag der [illegible] fuer Naturforschung

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Higher plants and several photosyn[illegible] contain the plastidic 1-deoxy-D-xylulose 5-phosphate /[illegible]-**erythritol 4-phosphate** pathway (DOXP/MEP pat[illegible] [illegible]soprenoid biosynthesis. The first four **enzymes** [illegible] their genes are known of this novel pathway. All of th[illegible] **enzymes** of this isoprenoid pathway are potential [illegible] new classes of herbicides. Since the DOXP/MEP pathway also [illegible] several pathogenic **bacteria**, such as Mycobacterium [illegible], and in the malaria **parasite** Plasmodium falciparum, [illegible]tors and potential herbicides of the DOXP/MEP pathw[illegible] are also potential drugs against pathogenic **bacteria** and [illegible] **parasite**. Plants with their easily to handl[illegible] MEP-pathway are thus very suitable **test**-systems also for new drugs [illegible] [illegible]thogenic **bacteria** and the malaria **parasite** [illegible] particular security measures are required. [illegible], the antibiotic herbicide fosmidomycin specifically inhibit[illegible] [illegible]ly the DOXP reductoisomerase in plants, but also that in **bacteria** [illegible] the **parasite** P. falciparum, and cures malaria-[illegible] mice. This is the first successful application of a herb[illegible] the novel isoprenoid pathway as a possible drug against malaria.

REFERENCE COUNT: 40 THERE AR[illegible] REFERENCES AVAILABLE FOR THIS RECORD. [illegible] AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER: 2000:615[illegible] H[illegible]

DOCUMENT NUMBER: 132:3[illegible]

TITLE: Characterisa[illegible] gene located between the class II re[illegible] genes in the human MHC

AUTHOR S : Aguado, B.; [illegible]

CORPORATE SOURCE: MRC Immunoche[illegible], Oxford University, Oxford, OX1 3QU, UK

SOURCE: HLA: Genetic [illegible] HLA Functional and Medical Implication, [illegible] of the International

Histocompatibility [illegible] and [illegible], 11th, Saint-Malo [illegible], France, 1997 [illegible], Meeting Date 1996 [illegible]. Editor(s): Charron, Dominique. [illegible] and Scientific International Publisher: [illegible]. CODEN: [illegible]

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The novel gene G15 encodes a [illegible] protein with a predicted mol. wt. of about 32 kDa which contains [illegible] transmembrane segments. The G15 gene is a single copy gene, [illegible] cell lines U937, Molt4 and Raji cells. The protein shows homol. with [illegible] **enzyme** LPAAT (1-acyl-sn-**glycerol-3-phosphate** acyltransferase lysophosphatidic [illegible] transferase) from several **bacteria**. The authors expressed G15 [illegible] **insect** cells using the baculovirus system and [illegible] demonstrate by enzymic **assays** whether G15 is the human [illegible] identify the cellular localization of the **enzyme**.

REFERENCE COUNT: 11 THERE ARE [illegible] REFERENCES AVAILABLE FOR THIS RECORD. [illegible] AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER: 1999:[illegible] HCAPLUS

DOCUMENT NUMBER: 132:148591

TITLE: Determination [illegible] **trehalose-6-phosphate** levels [illegible] Saccharomyces cerevisiae, using Bacillus [illegible] phosphotrehalase

AUTHOR(S): Van Vaeck, C.; [illegible]; Bonini, B.; Van Dijck, P.; Thevelein, J. M.

CORPORATE SOURCE: Laboratory of [illegible] Cell Biology, Institute of Botany and [illegible], Louvain, Belg.

SOURCE: Mededelingen - [illegible] Landbouwkundige en Toegepaste Biologische Wetenschappen (Universiteit Gent) (1999), 64(5b), 647-[illegible]. CODEN: MFLBER; [illegible]-7503

PUBLISHER: Universiteit Gent, [illegible] Landbouwkundige en Toegepaste [illegible] Wetenschappen

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The disaccharide trehalose is a [illegible] determinant of stress resistance in several organisms. It was found in **bacteria**, yeast, **fungi** and in certain invertebrate [illegible] species. Deletion of the 1st **enzyme** of trehalose synthesis, [illegible], in yeasts results in a pleiotropic phenotype including [illegible] of trehalose, deficiency in growth on rapidly fermentable sugars [illegible] loss of stress resistance. To study the changes of **trehalose-6-phosphate** (Tre6P), the precursor of trehalose, [illegible] type cells and in yeast cells transformed with TPS1 homologs from [illegible] organisms, the authors developed a novel Tre6P **assay**. The authors' [illegible] show that complementation of a tps1.DELTA. [illegible] homologs from other organisms restores growth, but not proper [illegible] sugar influx into glycolysis.

REFERENCE COUNT: 5 THERE ARE [illegible] REFERENCES AVAILABLE FOR THIS RECORD. [illegible] AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER: 1999:[illegible] HCAPLUS

DOCUMENT NUMBER: 131:[illegible]

TITLE: Plant [illegible] [illegible]ase

INVENTOR(S): Smirnoff, Nich[illegible]; [illegible]

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PATENT ASSIGNEE(S):      Ascorbex Lim[illegible] [illegible] Technology Southwest Limited
SOURCE:                  PCT Int. Appl., [illegible]
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE            APPLICATION NO.  DATE
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     WO 9933995        A1   1999[illegible]    [illegible]-GB39[illegible]  1998[illegible]
         W: AL, AM, AT, AU, AZ, BA, [illegible], [illegible], BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, [illegible], [illegible], HU, ID, IL, IN, IS, JP, KE,
            KG, KP, KR, KZ, LC, LK, [illegible], [illegible], LU, LV, MD, MG, MK, MN, MW,
            MX, NO, NZ, PL, PT, RO, [illegible], [illegible], SG, SI, SK, SL, TJ, TM, TR,
            TT, UA, UG, US, UZ, VN, [illegible], [illegible], AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, [illegible], [illegible], AT, BE, CH, CY, DE, DK, ES,
            FI, FR, GB, GR, IE, IT, [illegible], [illegible], PT, SE, BF, BJ, CF, CG, CI,
            CM, GA, GN, GW, ML, MR, [illegible], [illegible], TG
     CA 2316990        AA   19990708        [illegible]-2316990  19981223
     AU 9917752        A1   19990719        [illegible]-17752    19981223
     EP 1042486        A1   20001011        [illegible]-962628   19981223
         R: AT, BE, CH, DE, DK, ES, FR, [illegible], IT, LI, NL, SE, PT, IE, FI
     JP 2002508155     T2   20020319        [illegible]-526651   19981223
PRIORITY APPLN. INFO.:                      [illegible]-[illegible]55     A  19971223
                                            [illegible]-1386     A  19980407
                                            [illegible]-[illegible]     A  19980417
                                            [illegible]-[illegible]903   W  19981223
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AB This invention presents and char[illegible] [illegible] plant L-galactose dehydrogenase, an **enzyme** which catalyzes the conv[illegible] [illegible] L-galactose to L-galactonolactone. The **enzyme** is [illegible]-dependent and the catalytic conversion is an oxidn. [illegible] at C1. The N-terminal sequence of the mature form of L-galactos[illegible] [illegible]nase from pea is provided. The invention further provides: (1) an [illegible] plant, **bacteria**, **fungi**, algae or mammal) engineered [illegible] L-galactose dehydrogenase; (2) a L-galactose de[illegible]nase gene-specific probe used to monitor gene presence; (3) a diagn[illegible] **test**, **assay** or monitoring method using the L-gala[illegible] dehydrogenase polypeptide; (4) a multi-**enzyme** pathway or method of p[illegible] L-ascorbic acid, wherein one step is catalyzed by L-[illegible] dehydrogenase; (5) a dietary supplement comprising ascorbic a[illegible] [illegible] organism, preferably a plant, that contains increased levels of a[illegible] acid; (7) use of L-galactose dehydrogenase antisense DNA to down-[illegible] the **enzyme**; and (8) a herbicidal compn. comprising a [illegible] that inhibits L-galactose dehydrogenase.

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REFERENCE COUNT:         3     THERE ARE [illegible] REFERENCES AVAILABLE FOR THIS
                               RECORD. [illegible] AVAILABLE IN THE RE FORMAT

L19  ANSWER 11 OF 15  HCAPLUS  COPYRIGHT [illegible]
ACCESSION NUMBER:        1998:246371  H[illegible]
DOCUMENT NUMBER:         129:6481[illegible]
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TITLE: **Trehalose-6-phosphate phosphatases** [illegible] [illegible]psis thaliana: identificati[illegible] [illegible]nal complementation of the yeast tps2 m[illegible]

AUTHOR(S): Vogel, Guid[illegible]; A[illegible], Roger A.; Muller, Joachim; Boller, Thomas; [illegible], Andres

CORPORATE SOURCE: Botanisches Ins[illegible], Universitat Basel, Basel, CH-4056, Swit[illegible]

SOURCE: Plant [illegible]
CODEN: [illegible] ; [illegible] - 41[illegible]
PUBLISHER: Blackwell [illegible]
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is currently thought that [illegible] plants lack the capacity to synthesize trehalose, a common [illegible] bacteria, fungi and invertebrates that app[illegible] a major role in desiccation tolerance. Attempts [illegible] been made to render plants more drought-resistant by the ex[illegible] microbial genes for trehalose synthesis. It is demonstrated [illegible] Arabidopsis thaliana itself possesses genes for at least one [illegible] enzymes required for trehalose synthesis, trehalose-6-phosphate phosphatase. The yeast tps2 mut[illegible], [illegible] lacks this enzyme, is heat-sensitive, and Ara[illegible] cDNA able to complement this effect has been screened for. [illegible] the yeast transformants that grew at 38.[illegible] also able to produce trehalose. All of these express[illegible] Arabidopsis cDNA, either AtTPPA or AtTPPB, which are [illegible] the C-terminal part of the yeast TPS2 gene and other microb[illegible] trehalose-6-phosphate phosphatases. Yeast tps[illegible] expressing AtTPPA or AtTPPB contained trehalose-6-phosphate phosphatase activity that [illegible] measured both in vivo and in vitro. The enzyme [illegible] sphorylated trehalose-6-phosphate but not glucose-6-phosphate or sucrose-6-ph[illegible]. Both genes are expressed in flowers and young developing tiss[illegible] [illegible]dopsis. The finding of these novel Arabidopsis genes for trehalose-6-phosphate phosphatase strongly ind[illegible] that a pathway for trehalose biosynthesis exists [illegible].

IT 9025-72-3, Trehalose-6-phosphate phosphatase
RL: PRP (Properties)
(trehalose-6-phosphate phosphatases from Arabidopsis th[illegible] identification by functional complementation of y[illegible] mutant)

L13 ANSWER 12 OF 15 HCAPLUS COPYRIGHT [illegible]

ACCESSION NUMBER: 1993:230685 H[illegible]
DOCUMENT NUMBER: 118:230685
TITLE: Effect of en[illegible] bacteria on mitochondrial [illegible] activities in the weevil Sitophilus ory[illegible] ([illegible]ptera:Curculionidae)
AUTHOR(S): Heddi, A.; [illegible]; Nardon, P.
CORPORATE SOURCE: Lab. Biol. App[illegible] Lyon, Villeurbanne, 69621, Fr.
SOURCE: Insect Biochem. [illegible] Molecular Biology (1993), 23(3), 403-1[illegible]
CODEN: IBMBES; [illegible] -65-1748
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various mitochondrial enzymic a[illegible] were investigated in symbiotic and aposymbiotic larvae and adults [illegible]philus oryzae. Six enzymes were assayed: cytochrom[illegible], succinate cytochrome c reductase, glycerol 3-phosphate cytochrome c reductase, isocitr[illegible]nase, pyruvate dehydrogenase, and .alpha.-ketoglutarate dehyd[illegible]. The specific activities of all these enzymes were higher in mi[illegible] isolated from symbiotic larvae than those [illegible] aposymbiotic larvae. In adults, the differences in enzym[illegible] activi[illegible] symbiotic and aposymbiotic

SOURCE: Plant Journal (19[illegible]), 1[illegible], 6[illegible]
CODEN: PLJUED; ISSN: 0960-7412
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is currently thought that most flowering plants lack the capacity to synthesize trehalose, a common disaccharide of **bacteria**, **fungi** and invertebrates that appears to play a major role in desiccation tolerance. Attempts have therefore been made to render plants more drought-resistant by the expression of microbial genes for trehalose synthesis. It is demonstrated here that Arabidopsis thaliana itself possesses genes for at least one of the **enzymes** required for trehalose synthesis, **trehalose-6-phosphate phosphatase**. The yeast tps2 mutant, which lacks this **enzyme**, is heat-sensitive, and Arabidopsis cDNA able to complement this effect has been **screened** for. Half of the yeast transformants that grew at [illegible] were also able to produce trehalose. All of these expressed one of two Arabidopsis cDNA, either AtTPPA or AtTPPB, which are both homologous to the C-terminal part of the yeast TPS2 gene and other microbial **trehalose-6-phosphate phosphatases**. Yeast tps2 mutants expressing AtTPPA or AtTPPB contained **trehalose-6-phosphate phosphatase** activity that could be measured both in vivo and in vitro. The **enzyme** dephosphorylated **trehalose-6-phosphate** but not glucose-6-phosphate or sucrose-6-phosphate. Both genes are expressed in flowers and young developing tissue of Arabidopsis. The finding of these novel Arabidopsis genes for **trehalose-6-phosphate phosphatase** strongly indicates that a pathway for trehalose biosynthesis exists in plants.

IT **9025-72-3, Trehalose-6-phosphate phosphatase**
RL: PRP (Properties)
(**trehalose-6-phosphate phosphatases** from Arabidopsis thaliana: identification by functional complementation of yeast tps2 mutant)

L14 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:230685 HCAPLUS
DOCUMENT NUMBER: 118:230685

TITLE: Effect of endocytobiotic **bacteria** on mitochondrial enzymic activities in the weevil Sitophilus oryzae (Coleoptera:Curculionidae)

AUTHOR(S): Heddi, A.; Lefebvre, F.; Nardon, P.
CORPORATE SOURCE: Lab. Biol. Appl., INSA Lyon, Villeurbanne, 69621, Fr.

SOURCE: Insect Biochemistry and Molecular Biology (1993), 23(3), 403-11
CODEN: IBMBES; ISSN: 0965-1748
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various mitochondrial enzymic activities were investigated in symbiotic and aposymbiotic larvae and adults of Sitophilus oryzae. Six **enzymes** were **assayed**: cytochrome c oxidase, succinate cytochrome c reductase, **glycerol 3-phosphate** cytochrome c reductase, isocitrate dehydrogenase, pyruvate dehydrogenase, and .alpha.-ketoglutarate dehydrogenase. The specific activities of all these **enzymes** were higher in mitochondria isolated from symbiotic larvae than those isolated from aposymbiotic larvae. In adults, the differences in enzymic activities between symbiotic and aposymbiotic

insects were [illegible]. [illegible]alpha.-[illegible] [illegible] activity was similar in the 2 strains, and pyruvate [illegible] activity was [illegible] in [illegible] strain. [illegible] the results [illegible] between symbiotic and aposymbiotic **insects** [illegible] that the presence [illegible] **bacteria** [illegible] the higher enzyme activities [illegible]. It is [illegible] that [illegible] bacterial metabolites could be implicated. These enzyme activities were also **tested** in symbiotic **bacteria** isolated from larval **bacteriome**. No activity was [illegible].

L13 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:124394 HCAPLUS
DOCUMENT NUMBER: 116:124394
TITLE: Target gene-complemented microorganisms for identification of **antiparasite** drugs
INVENTOR(S): Klein, Ronald D.; Geary, Timothy G.
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117260	A1	19911114	WO 1991-US2767	19910425
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5179143	A	19920107	US 1990-517633	19900502
AU 9179750	A1	19911127	AU 1991-79750	19910425

PRIORITY APPLN. INFO.: US 1990-517633 19900502
WO 1991-US2767 19910425

AB A method for identifying **antiparasitic** drugs comprises exposing **parasite** gene-complemented microorganisms to the **test** compd. and detg. microbial viability. An Escherichia coli mutant deficient in both phosphofructokinase (PFK) **enzymes** was used to clone the PFK cDNA of Haemonchus contortus by complementation. The cDNA was sequenced.

L13 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:90393 HCAPLUS
DOCUMENT NUMBER: 108:90393
TITLE: A sensitive and efficient isoenzyme technique for small arthropods and other invertebrates
AUTHOR(S): Easteal, Simon; Boussy, Ian A.
CORPORATE SOURCE: Res. Sch. Biol. Sci., Aust. Natl. Univ., Canberra, 2601, Australia
SOURCE: Bulletin of Entomological Research (1987), 77(3), 407-15
CODEN: BUENAZ; ISSN: 0007-4853
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An electrophoretic method for the study of **enzyme** variation, which uses cellulose acetate sheets with an agar overlay for staining, the use of a very good general purpose buffer (citric-aminopropylmorpholine), and the use of sodium azide as a **bacteriocide** to allow

[illegible] for their storage or trans. as solns. are described. **Tests** are reported of the technique on Tetrahymena [illegible], Aedes aegypti, and several species of Drosophila. The technique offers sensitivity equal to or greater than starch or polyacrylamide gel electrophoresis and [illegible] [illegible] very small organisms, allowing [illegible] the **testing** of single individuals for [illegible] nos. of **enzymes** or the **testing** of fewer **enzymes** under different [illegible] conditions, [illegible] [illegible] variation [illegible]. The technique is efficient with respect to time and materials, and safer than conventional methods.

IT 9075-65-4, Glycerol 3-phosphate dehydrogenase
RL: BIOL (Biological study)
isoenzymes, detection of, by cellulose acetate electrophoresis

L16 ANSWER 16 OF 16 HCAPLUS COPYRIGHT [illegible] ACS
ACCESSION NUMBER: [illegible] HCAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: Effects of some antitumor agents on growth and glycolytic **enzymes** of the flagellate Crithidia
AUTHOR(S): Bacchi, Cyrus J.; Ciaccio, Edward I.; Koren, Lois E.
CORPORATE SOURCE: Haskins Lab., New York, NY, USA
SOURCE: Journal of Bacteriology (1969), 98(1), 23-8
CODEN: JOBAAY; ISSN: [illegible]
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some antitumor agents known to specifically inhibit certain tumor cell **enzymes** were examd. for activity against glycolytic **enzymes** and for growth of the **insect** trypanosomatid, C. fasciculata. The cytoplasmic **enzymes** hexokinase, .alpha.-glycerophosphate dehydrogenase, malic dehydrogenase, and glucose-6-phosphate dehydrogenase were **tested**. Agaricic acid (2-hydroxy-1,2,3-nonadecanetricarboxylic acid) was highly inhibitory ([illegible]-100%) to malic and .alpha.-glycerophosphate dehydrogenases at (approx.[illegible] .times. 10-5M; 2-(p-hydroxyphenyl)-2-phenylpropane (2 .times. 10-4M) and 5,6-dichloro-2-benzoxazolinone (5 .times. 10-4M) were less effective (50% inhibition) against them. The antiprotozoal agents primaquine (4 .times. 10-4M) and Melarsoprol (8 .times. 10-4M) were 30-41% inhibitory. Agaricic acid, 2-(p-hydroxyphenyl)-2-phenylpropane, and 5,6-dichloro-2-benzoxazolinone inhibited growth of Crithidia at less than 10-4M. Eight other **test** compds. from the Cancer Chemotherapy National Service Center (CCNSC) were not toxic to cell growth, although two (4-biphenylcarboxylic acid and 1-(p-chlorobenzyl)-2-ethyl-5-methylindole-3-acetic acid) inhibited Crithidia .alpha.-glycerophosphate dehydrogenase below 1M. All of the compds. used specifically inhibited cancer cell .alpha.-glycerophosphate dehydrogenase. The corresponding **enzyme** in pathogenic African trypanosomes is important in their terminal respiration. C. fasciculata may be useful in preliminary evaluation of chemotherapeutic agents as potential trypanocides.

IT 9075-65-4, Glycerol phosphate dehydrogenase
in Crithidia fasciculata, neoplasm inhibitor effect on